

What is claimed is:

1. An oligonucleotide having a sequence complementary to a sequence of a ribonucleic acid encoding a heparanase, wherein:

- 5 (a) the oligonucleotide hybridizes with the ribonucleic acid under conditions of high stringency and is between 10 and 40 nucleotides in length;
- 10 (b) the internucleoside linkages of the oligonucleotide comprise at least one phosphorothioate linkage; and
- 15 (c) hybridization of the oligonucleotide to the ribonucleic acid inhibits expression of the heparanase, wherein inhibition of heparanase expression means at least a 50% reduction in the quantity of heparanase as follows: (a) a T24 bladder carcinoma cell is exposed to a complex of the oligonucleotide and lipofectin at an oligonucleotide concentration of 1 μ M and a lipofectin concentration of 10 μ g/ml for 5 hours at 37°C, (b) the complex is completely removed after such exposure, (c) 19 hours later the cell is scraped, washed and extracted in lysis buffer,
- 20 (d) the nucleus of the cell is removed by centrifugation, (e) the cytoplasmic proteins in the resulting supernatant are separated according to mass by sodium dodecyl sulphate polyacrylamide gel electrophoresis, (f) the protein is transferred to a polyvinylidene difluoride membrane that is incubated at room temperature for 1-2 hours in incubation solution (g) the
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membrane is exposed to 1 µg/ml of an antibody
directed against heparanase at 4°C for 12 hours,
(h) the membrane is exposed to wash buffer and
incubated for 1 hour at room temperature in
blocking buffer comprising a 1:3,000 dilution of
a peroxidase-conjugated secondary antibody
directed against an epitope on the antibody
directed against heparanase, (i) the membrane is
exposed to a chemiluminescent cyclic
diacylhydrazide and the oxidation of the cyclic
diacylhydrazide by the peroxidase is detected as
a chemiluminescent signal, and (j) the signal is
quantitated by laser-scanning densitometry as a
measure of the amount of heparanase expressed
calculated as a percentage of heparanase
expression in an untreated cell.

- 5 2. The oligonucleotide of claim 1, wherein the
10 oligonucleotide comprises deoxyribonucleotides.
- 15 3. The oligonucleotide of claim 1, wherein the
20 oligonucleotide comprises ribonucleotides.
- 25 4. The oligonucleotide of claim 1, wherein every
internucleoside linkage is a phosphorothioate linkage.
- 30 5. The oligonucleotide of claim 1, wherein the
oligonucleotide is between 15 and 25 nucleotides in
length.
6. The oligonucleotide of claim 1, wherein the
oligonucleotide is about 20 nucleotides in length.

Sub A2 5
7. The oligonucleotide of claim 1, wherein the sequence of the oligonucleotide is selected from the following:

- (a) CCCCAGGAGCAGCAGCAGCA (SEQ ID NO:3);
- (b) GTCCAGGAGCACTGAGCAT (SEQ ID NO:4); and
- (c) AGGTGGACTTCTTAGAAGT (SEQ ID NO:5).

Sub A2 10
8. The oligonucleotide of claim 1, wherein the oligonucleotide further comprises a modified internucleoside linkage.

Sub A3 9
The oligonucleotide of claim 8, wherein the modified internucleoside linkage is a peptide-nucleic acid linkage, a morpholino linkage, a phosphodiester linkage or a stereo-regular phosphorothioate.

Sub A3 20
10. The oligonucleotide of claim 1, wherein the oligonucleotide further comprises a modified sugar moiety.

11. The oligonucleotide of claim 10, wherein the modified sugar moiety is 2'-O-alkyl oligoribonucleotide.

25 12. The oligonucleotide of claim 1, wherein the oligonucleotide further comprises a modified nucleobase.

30 13. The oligonucleotide of claim 12, wherein the modified nucleobase is a 5-methyl pyrimidine or a 5-propynyl pyrimidine.

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14. The oligonucleotide of claim 1, wherein the heparanase
is a human heparanase.
15. A method of inhibiting expression of a heparanase in
a cell comprising contacting the cell with the
oligonucleotide of claim 1 under conditions such that
the oligonucleotide hybridizes with mRNA encoding the
heparanase so as to thereby inhibit the expression of
the heparanase.
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16. The method of claim 15, wherein the cell is a cancer
cell.
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17. A composition comprising the oligonucleotide of claim
1 in an amount effective to inhibit expression of a
heparanase in a cell and a carrier.
18. The composition of claim 17, wherein the
oligonucleotide and the carrier are capable of passing
through a cell membrane.
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19. The composition of claim 18, wherein the carrier
comprises a membrane-permeable cationic reagent.
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20. The composition of claim 19, wherein the cationic
reagent is lipofectin.
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21. A method of treating a tumor in a subject which
comprises administering to the subject an amount of
the oligonucleotide of claim 1 effective to inhibit
expression of a heparanase in the subject and thereby
treat the tumor.

22. A method of treating a subject which comprises
administering to the subject an amount of the
oligonucleotide of claim 1 effective to inhibit
expression of a heparanase in the subject and thereby
treat the subject.

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23. The method of claim 21 or 22, wherein the subject is
a human being.

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24. The method of claim 21, wherein the treatment of the
tumor is effected by reducing tumor growth.

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25. The method of claim 21, wherein the treatment of the
tumor is effected by reducing tumor metastasis.

26. The method of claim 21, wherein the treatment of the
tumor is effected by reducing angiogenesis.

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27. Use of the oligonucleotide of claim 1 for the
preparation of a pharmaceutical composition for
treating a tumor in a subject which comprises admixing
the oligonucleotide in an amount effective to inhibit
expression of a heparanase in the subject, with a
pharmaceutical carrier.

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28. An oligonucleotide having a sequence complementary to
a sequence of a ribonucleic acid encoding a
heparanase, wherein:
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(a) the oligonucleotide hybridizes with the
ribonucleic acid under conditions of high
stringency and is between 10 and 40 nucleotides

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- (b) in length; the internucleoside linkages of the oligonucleotide comprise at least one phosphorothioate linkage; and

(c) hybridization of the oligonucleotide to the ribonucleic acid inhibits expression of the heparanase.

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